Prerenal uremia induced by severe diarrhea due to colon adenoma: a case of McKittrick–Wheelock syndrome in an elderly patient

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Abstract McKittrick–Wheelock syndrome can be successfully treated by emergent dialysis, prescription of bicarbonate, and endoscopic submucosal dissection, which allow elderly people suffering from this syndrome to maintain their activities of daily living. In patients with this syndrome, a large colonic villous adenoma secretes excessive amounts of mucus and causes severe electrolyte depletion and dehydration. An 81-year-old man who had been suffering from chronic renal failure (creatinine 256.4 $\mu\text{mol/L}$), hypertension, and arrhythmia presented with frequent mucous diarrhea for a month. He was hospitalized for appetite loss, vomiting, general fatigue, and acute renal failure. His blood tests and blood gas analysis revealed urea nitrogen 58.9 mmol/L, creatinine 954.7 $\mu\text{mol/L}$, pH 7.13, and a base excess of -20.1 mmol/L. Although his symptoms were improved by the emergent dialysis and rehydration, he suffered a relapse only 4 days after he was discharged. At the second admission, a near-circumferential tumor was found in the rectum by the colonoscopy, which was pathologically confirmed as a villous adenoma. Considering his age and complications, endoscopic submucosal dissection was selected, and internal use of sodium bicarbonate was prescribed. Diarrhea and appetite loss were improved by these treatments, and the creatinine level was also improved to 168.0 $\mu\text{mol/L}$.

Keywords Diarrhea · Villous adenoma · Acute renal failure · McKittrick–Wheelock syndrome

Introduction

McKittrick and Wheelock were the first to report a large colon villous adenoma with fluid and electrolyte imbalances [1], so this clinical condition is now referred to as McKittrick–Wheelock syndrome. Although most colonic tumors are asymptomatic or accompanied by hematochezia, villous adenoma is known to cause severe diarrhea. This diarrhea sometimes induces acute prerenal uremia due to the dehydration that results from excessive fluid depletion.

We experienced a case of McKittrick–Wheelock syndrome, and our treatment—a curative treatment for the tumor itself and supportive measures for the electrolyte and fluid imbalances—successfully ameliorated the patient's condition.

Case report

An 81-year-old man had been suffering from chronic renal failure, hypertension, and arrhythmia. He had been prescribed angiotensin type 1 receptor blocker (ARB), calcium antagonist, and warfarin for many years. His serum creatinine (Cr) level was 256.4 $\mu\text{mol/L}$ and potassium level was 5.7 mmol/L at the beginning of June. At the end of that month, he felt sick and grew concerned about his frequent mucous diarrhea. He was taken to the emergency hospital for appetite loss, vomiting, and general fatigue on June 30, and was diagnosed with prerenal uremia accompanied by marked metabolic acidosis with an increased anion gap due

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to severe dehydration caused by the frequent diarrhea. He had sub fever and did not have significant abdominal rebound tenderness. His blood pressure (BP) was 120/75 mmHg, while his blood tests and blood gas analysis revealed hemoglobin (Hb) 101 g/L, urea nitrogen (BUN) 58.9 mmol/L, Cr 954.7 μ mol/L, sodium 135 mmol/L, potassium 4.5 mmol/L, pH 7.13 HCO₃ 7.2 mmol/L, and base excess −20.1 mmol/L (Table 1). Rehydration solution containing sodium bicarbonate was administered immediately. Since oliguria persisted for more than 24 h under this treatment, he was transferred to our hospital for emergent hemodialysis. After undergoing dialysis on July 2 and 8, his condition and the blood test results improved (BUN 16.4 mmol/L, Cr 273.2 μ mol/L). Although he still had mild diarrhea, he was discharged on July 25.

Due to general fatigue and appetite loss, he was taken by ambulance to the hospital again on July 29, only 4 days after the discharge. He lost 4.5 kg in 4 days, and his blood pressure dropped to 85/54 mmHg. His blood test showed Hb 142 g/L, BUN 52.1 mmol/L, and Cr 1005 μ mol/L, and blood gas revealed a pH of 7.082 (Table 1). These data suggested serious hemoconcentration and uremia due to severe dehydration. Furthermore, carcinoembryonic antigen (CEA) was high (9.2 ng/mL). Dialysis was performed on July 29 and 30, and his general condition recovered. Since his stool was jellylike or mucous, and his CEA was high, a colonoscopy was done on August 4. A near-circumferential easy-bleeding tumor was found in the rectum (Fig. 1). The tumor tissue was biopsied (Fig. 2), and he was diagnosed with tubulovillous adenoma (group 3). It

was suggested that his diarrhea was caused by excessive mucus secretion by the tumor. Abdominal plain CT showed irregular near-circumferential thickening of the rectum wall without lymph-node swelling (Fig. 3).

To provide supportive care, sodium bicarbonate (1.5 g per day) was administered on August 12, and this improved his condition and appetite. The blood test on September 2 revealed even better results (BUN 9.28 mmol/L, Cr 168.0 μ mol/L) than those at the beginning of June, though the diarrhea persisted.

Considering his age and condition, endoscopic submucosal dissection (ESD) was chosen for the adenoma resection instead of open abdominal surgery. Multiple partial ablations were planned, and he was transferred to Keio University Hospital. The first endoscopic submucosal dissection was done on September 30. Villous adenocarcinoma (group 5) was detected from the dissected tissue. The dissection was done in incremental steps at intervals of a few months. After the first ablation, the tumor size decreased by 40 %, and this partial resection reduced the frequency of diarrhea. Since then, resection has been performed three times, and there has been no relapse of diarrhea with renal failure for more than a year since the first admission.

Discussion

Since it was first reported by McKittrick and Wheelock in 1954 [1], several cases characterized by a large villous

Table 1 Laboratory data during hospitalization; emergent dialysis ameliorated uremia, and sodium carbonate administration maintained electrolyte balances

Date	First admission				Second admission					
	July				August					September
	2	15	22	29	4	8	12	15	22	2
Weight (kg)	43.6	43.3	43.2	38.6	39.8			42.3	43.4	44.3
BP (mmHg)	120/75	100/55	105/62	85/54	96/66	100/62	96/68	112/56	100/50	108/56
Hb (g/L)	101	97		142	105	102			90	91
BUN (mmol/L)	59	19	16	52	39	22		15	11	9
Cr (μ mol/L)	955	354	274	1008	592	380		212	177	168
UA (μ mol/L)	767	559	399		642	410		488	482	470
Na (mmol/L)	135	133	139	136	133	132	132	136	138	138
K (mmol/L)	4.5	2.5	3.1	4.6	2.6	3.1		3.1	3.6	4
Cl (mmol/L)	96	99	108	90	97	99	103	107	106	105
pH	7.131			7.082			7.391			
pCO ₂ (mmHg)	22.2			24.7			24.1			
pO ₂ (mmHg)	114.8			118			118.6			
BE (mmol/L)	−20.1			−21.2			−8.5			
HCO ₃ (mmol/L)	7.2			7.2			14.3			
Anion gap (mmol/L)	31.8			38.8			14.7

Fig. 1 Colonoscopy: easy-bleeding large rectal tumor

Fig. 2 Histopathological examination of the tumor biopsy from the patient's rectum: tubulovillous adenoma (group 3). Hematoxylin-eosin stain (×20)

Fig. 3 Plain CT of the abdomen: a near-circumferential tumor in the rectum, and no regional invasion or adjacent lymphadenopathy

adenoma with severe diarrhea leading to electrolyte imbalances have been reported. Generally, diarrhea causes metabolic acidosis without an increased anion gap due to loss of potassium and bicarbonate from the colon. However, the pH range of McKittrick–Wheelock syndrome is wide, ranging from metabolic [2, 3] and respiratory alkalosis [4, 5] to metabolic acidosis [6–8]. Severe electrolyte depletion from diarrhea produces several secondary complications, including hyperventilation and renal failure. These complications and the extent of the diarrhea may produce a variety of acid–base imbalances. Our case presented metabolic acidosis with a striking increase in the anion gap. Acute exacerbation of renal failure and poor dietary intake may have promoted the accumulation of fixed acids and ketones. Additionally, in our case, the use of ARB may also have accelerated acute renal failure under hypovolemic conditions.

Renin–angiotensin–aldosterone system (RAAS) blockers have cardioprotective and renoprotective effects in many clinical settings, and this renoprotective effect is attributable to reduced intraglomerular pressure by efferent arteriolar dilatation. In settings where glomerular filtration is maintained by efferent arteriolar constriction, such as in cases of diabetes, CHF, diarrhea, and vomiting, its vasodilatory action can induce acute kidney injury [9–11].

A variety of mechanisms have been postulated for the secretion of villous adenoma. Cholera toxin, a famous cause of severe diarrhea, is water and electrolyte secretion caused by the stimulation of prostaglandin synthesis and adenylate cyclase activation [12–14]. Studies have shown that (1) the cyclic AMP content in a secretory tumor is higher than that in a nonsecretory tumor and normal mucosa [15], and (2) prostaglandin E2 levels in the rectal fluid of a villous tumor are high [16]. COX2 is reportedly overexpressed in colorectal adenoma and adenocarcinoma [17]. Indomethacin, a cyclooxygenase (COX) inhibitor, suppresses diarrhea as well as the prostaglandin E2 level [16, 18]. However, the administration of these drugs is controversial because of their gastrointestinal and cardiovascular side effects [19–21].

The secretory properties of villous adenoma are still controversial. Villous adenoma mainly induce diarrhea in the distal colon, though the presence of this tumor in the proximal colon only infrequently leads to diarrhea [22]. Extract from villous adenoma influences the movement of electrolytes and fluid across the proximal colon, but it does not affect such movement across the distal colon [23]. Physiologically, reabsorption and secretion mainly occur in the proximal colon [24], and partial secretion by villous adenoma may indicate that it induces diarrhea via a paracrine mechanism.

McKittrick–Wheelock syndrome requires immediate treatment of prerenal uremia due to severe dehydration and

electrolyte depletion. In rare cases, dialysis is also required [25, 26]. In our case, dialysis was chosen as a means to ameliorate the electrolyte imbalances caused by both severe diarrhea and preexisting chronic renal failure. Along with the immediate rehydration and dialysis, administration of bicarbonate also helped to stabilize the patient's condition. Administration of a small amount of bicarbonate may ameliorate appetite loss by inhibiting the aggravation of acidosis.

Untreated McKittrick–Wheelock syndrome is known to be fatal [27]. Large villous adenomas frequently contain adenocarcinoma [28]. The initial diagnosis in our case was of villous adenoma group 3, and the ESD tissue showed the presence of adenocarcinoma. Though colectomy is usually chosen for the treatment of colon cancer, open abdominal surgery was difficult in our case because of the patient's advanced age and complications. Fortunately, no distal metastasis was found in preoperative examinations. ESD has been reported to be a safe and effective treatment for giant tumor [29], so we chose ESD instead of open surgery. For over a year from the first dissection, there was no recurrence of the diarrhea and his activities of daily living (ADL) were maintained. ESD could be one of the best indications for patients with this syndrome who have many complications.

Treatment selection is somewhat problematic for elderly patients. Multiple complications in such patients restrict the range of medications and operative procedures available. Long-term admission and invasive treatments for the elderly also lead to delirium, and drain the patient's energy [30, 31]. In our case, we implemented three steps for the treatment of McKittrick–Wheelock syndrome, namely (1) hemodialysis for the emergent correction of fluid and electrolyte imbalances, (2) sodium bicarbonate to maintain the patient's condition as a conservative treatment, followed by (3) ESD for the tumor resection. Emergent dialysis is an effective treatment for the problems caused by acute uremia. Bicarbonate administration ameliorated the symptoms of renal failure, such as appetite loss and general fatigue, but it did not reduce the frequency of diarrhea. ESD is an excellent method, as only short-term hospital admission of the patient is needed, and because it does not require specific anesthesia.

To summarize, we experienced a case of McKittrick–Wheelock syndrome. Our case was ameliorated by emergent dialysis, sodium bicarbonate administration, and ESD. These three less-invasive steps enabled us to maintain the ADL of an elderly McKittrick–Wheelock syndrome patient in the long run.

Conflict of interest All the authors have declared no competing interest.

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